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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,716	BONNEFOY ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12 and 15-20* is/are pending in the application.

4a) Of the above claim(s) *15-17 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-10, 12, and 15-20 are pending.

2. Newly submitted claim 20 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 20 is drawn to a method of selecting an inhibitory antibody which differs with respect to the method steps and end points of the method of treatment using the antibody. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 20 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 15-17 and 20 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-10, 12 and 18 and 19 are being acted upon in this Office Action.

5. In view of the amendment filed 10/6/03, the following rejection remains.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 6-7 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "the framework of the heavy chain includes the amino acid residues" in claim 6 is indefinite and ambiguous because the specific amino acid residues at position 49, 66, 76, 77 and 94 are not recited in the claim. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

Likewise, the "amino acid residues from the murine antibody at position 64" is ambiguous and indefinite because the specific amino acid residue from the framework of the light

chain of which murine antibody is not recited in the claim. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

Applicants' arguments filed 10/6/03 have been fully considered but are not found persuasive.

Applicants' position is that claims have been amended and claim11, 13 and 14 have been amended. However, the specific amino acid residues at the specific positions as recited in claims 6 and 7 are not specified. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-10, 12, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for:

(1) An antibody that binds specifically to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO: 11 and CDRH3 consisting of the amino acid sequence FID of SEQ ID NO: 13 for diagnostic purpose;

(2) A humanized antibody or chimeric antibody that binds specifically to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence

EIRLKSDNYATHYAESVKG of SEQ ID NO: 11 and CDRH3 consisting of the amino acid sequence FID of SEQ ID NO: 13;

(3) An antibody that binds specifically to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO: 11, CDRH3 consisting of the amino acid sequence FID of SEQ ID NO: 13 and has an affinity constant equal to or greater than $1x10^{9}$ Ka Mo^{-1};

(4) A humanized antibody that binds specifically to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO: 11, CDRH3 consisting of the amino acid sequence FID of SEQ ID NO: 13, and the human variable heavy chain framework amino acid sequence retains the mouse heavy chain variable framework amino acids at positions 49, 66, 76, 77 and 94,

(5) A humanized antibody that binds specifically to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO: 11, CDRH3 consisting of the amino acid

sequence FID of SEQ ID NO: 13, and the human variable light chain framework amino acid sequence retains the mouse light chain variable framework amiño acids at positions 64;

(6) A antibody comprising one or both of the amino acid sequences encoded by the nucleic acid sequence according to SEQ ID NO: 1 and 2;

(7) A antibody comprising one or both of the amino acid sequences encoded by the nucleic acid sequence according to SEQ ID NO: 17 and 17;

(8) An antibody that binds specifically to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO: 11, CDRH3 consisting of the amino acid sequence FID of SEQ ID NO: 13 and a constant region consisting of an amino acid substitution at position from 248 to Ala and Gly to Ala at position of 250; and (9) A method of making any antibody mentioned above for diagnostic purpose and for screening for antibody which competitively inhibits the binding of any antibody mentioned above, **does not** reasonably provide enablement for: (1) a method of treatment or prophylaxis of *any* disorder such as the ones recited in claim 12 comprising administration of an antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9), EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) for treating arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis, eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies;

(2) *any* antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on

haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9), EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) in which the framework of the heavy chain includes any of the amino acid residues from any murine antibody at any of positions 49, 66, 76, 77 and 94,

(3) *any* antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9), EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) in which the framework of the light chain included any amino acid residues from any murine antibody at position 64.

(4) *any* pharmaceutical formulation comprising the antibody as set forth in claim 1 for treating or preventing any disorder such as arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis, eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies and

(5) *any* pharmaceutical formulation comprising the antibody as set forth in claim 1 in combination with any immunomodulatory or anti-inflammatory agent and a pharmaceutically acceptable excipient for treating or preventing any disorder such as arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis, eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only one monoclonal antibody that binds to CD23 comprising SEQ ID NO: 2 and SEQ ID NO: 1. The specification further discloses a humanized CD23 antibody and a chimeric antibody that binds to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1 consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO: 11 and CDRH3 consisting of the amino acid sequence FID of SEQ ID NO: 13. The specification further discloses that the said antibody has affinity constant (Ka) approximately 9 x 10^{10}/mol for screening for competitive inhibitor.

The specification does not teach how to make *any* antibody as set forth in claim 1 having undisclosed amino acid residues in the framework of the heavy chain at the positions 49, 66, 76, 77 and 94 or the antibody as set forth in claim 1 having the undisclosed amino acid residues at position 64 of the framework of light chain because there is insufficient guidance as which undisclosed amino acid residues to be includes at those positions and whether the resulting antibody maintain the structure and binding specificity as the antibody set forth in claim 1.

Abaza *et al*, of record, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular).

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion

which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al*, of record, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide.

Even if the antibody is limited to the one set forth in claim 1, there is insufficient guidance as how to treat or prevent any disease such as the ones recited in claim 12. Given the numerous diseases, there is no in vivo working example in the specification as filed demonstrating the claimed antibody could treat, much less prevent any disease. Autoimmune diseases such as the ones recited in claim 12 can be species- and model-dependent, it is not clear that the reliance on in vitro binding assays accurately reflects the relative efficacy of using any undisclosed antibody for the claimed therapeutic strategy.

Van Noort *et al* teach that induction of EAE with MBP does not result in the development of relapse and the clinical course may be different than that after treatment with other antigen such as SCH and PLP (See page 170, in particular). Further, there is no showing of treating any animal with the claimed antibody alone or in combination with any immunomodulatory or anti-inflammatory agent in the specification as filed demonstrating the claimed pharmaceutical composition and method is effective for treating or preventing a wide range of diseases from autoimmune disease to B cell malignancy.

With regard to autoimmune disease, Couzin *et al* teach that three major prevention trials have failed to stop autoimmune disorder such as type I diabetes (See entire document, Science 300: 1862-65, 2003).

With regard to B cell malignancies, Bodey et al teach that "while cancer vaccine trials have yielded tantalizing results, active immunotherapy has not yet become an established modality of anticancer therapy" (page 2665, column 2) and "the use of active specific immunotherapy (ASI) for cancer (cancer 'vaccines') is still in its scientific infancy despite several decades of clinical and basic research" (see page 2668, column 2, in particular). In the absence of in vivo data, it is unpredictable which disease would be treated by the claimed pharmaceutical composition or the claimed method. Further, treating any diseases in the absence of in vivo data is unpredictable since the antibody may have other functional properties, known or unknown, that

may make the antibody unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In addition, Spitler et al recognizes the lack of predictability of the nature of the art when she states, "ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: 'cancer vaccines don't work'. Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response" (page 1, paragraph 1).

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 10/6/03 have been fully considered but are not found persuasive.

Applicants' position is that claims have been amended and claim11, 13 and 14 have been amended.

However, amended claim 12 recites a method of treatment or prophylaxis of *any* disorder such as the ones recited in claim 12 comprising administration of an antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9), EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) for treating arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis,

eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies. Further, the specification does not teach how to make *any* antibody as set forth in claim 1 having undisclosed amino acid residues in the framework of the heavy chain at the positions 49, 66, 76, 77 and 94 or the antibody as set forth in claim 1 having the undisclosed amino acid residues at position 64 of the framework of light chain because there is insufficient guidance as which undisclosed amino acid residues to be includes at those positions and whether the resulting antibody maintain the structure and binding specificity as the antibody set forth in claim 1.

10. Claims 1-10, 12, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of treatment or prophylaxis of *any* disorder such as the ones recited in claim 12 comprising administration of an antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9), EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) for treating arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis, eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies;

(2) *any* antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9), EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) in which the framework of the heavy

chain includes any of the amino acid residues from any murine antibody at any of positions 49, 66, 76, 77 and 94,

(3) *any* antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9), EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) in which the framework of the light chain included any amino acid residues from any murine antibody at position 64.

(4) *any* pharmaceutical formulation comprising the antibody as set forth in claim 1 for treating or preventing any disorder such as arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis, eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies and

(5) *any* pharmaceutical formulation comprising the antibody as set forth in claim 1 in combination with any immunomodulatory or anti-inflammatory agent and a pharmaceutically acceptable excipient for treating or preventing any disorder such as arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis, eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies.

The specification discloses only one monoclonal antibody that binds to CD23 comprising SEQ ID NO: 2 encoded by the polynucleotide of SEQ ID NO: 1. The specification further discloses a humanized CD23 antibody and a chimeric antibody that binds to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells or soluble CD23 comprising light chain variable domains CDRL1, CDRL2, CDRL3, heavy chain variable domains CDRH1, CDRH2 and CDRH3 wherein CDRL1 consisting of the amino acid sequence RSSKSLLY KDGKTYLN of SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence LMSTRAS of SEQ ID NO: 5, CDRL3 consisting of the amino acid sequence QQLVEYPFT of SEQ ID NO: 7, CDRH1

consisting of the amino acid sequence GYWMS of SEQ ID NO: 9, CDRH2 consisting of the amino acid sequence EIRLKSDNYATHYAESVKG of SEQ ID NO: 11 and CDRH3 consisting of the amino acid sequence FID of SEQ ID NO: 13. The specification further discloses that the said antibody has affinity constant (Ka) of $9 \times 10^{10}/mol^{-1}$ for diagnostic purpose and for screening assays.

With the exception of the specific antibody mentioned above for diagnostic purpose and for screening assays, there is insufficient written description about the amino acid residues to be included in the claimed antibody as set forth in claims 6 and 7. Further, given the infinite number of diseases as set forth in claim 12, the method of treating using the specific antibody is not adequately described. It also follows that any pharmaceutical formulation comprising any undisclosed antibody mentioned above or in combination with any immunomodulatory or any anti-inflammatory agent is not adequately described.

Further, the specification discloses only one monoclonal antibody, one humanized antibody and one chimeric antibody that binds to CD23 which is a type II molecule expressed on haematopoietic cells for diagnostic and screening assays. Given the lack of a disclosure for treating a specific disease using the claimed antibody, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 10/6/03 have been fully considered but are not found persuasive.

Applicants' position is that claims have been amended and claim11, 13 and 14 have been amended.

However, amended claim 12 recites a method of treatment or prophylaxis of *any* disorder such as the ones recited in claim 12 comprising administration of an antibody which is comprises the amino acid sequence of each CDR shown below such that the antibody is capable of binding to the CD23 (FCεRII) type II molecule expressed on haematopoietic cells: RSSKSLLY KDGKTYLN which is CDRL1 (SEQ ID NO: 3), LMSTRAS which is CDRL2 (SEQ ID NO: 5), QQLVEYPFT which is CDRL3 (SEQ ID NO: 7), GYWMS which is CDRH1 (SEQ ID NO: 9),

EIRLKSDNYATHYAESVKG which is CDRH2 (SEQ ID NO: 11) and FID ....which is CDRH3 (SEQ ID NO: 13) for treating arthritis, lupus erythematosus, Hashimotos thyroiditis, multiple sclerosis, diabetes, uveitis, dermatitis, psoriasis, urticaria, nephritic syndrome, glomerulonephritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, Sjogren's syndrome, allergies, allergic asthma, intrinsic asthma, acute asthmatic exacerbation, rhinitis, eczema, GVH, COPA, insulitis, bronchitis (particularly chronic bronchitis), diabetes (particularly Type 1 diabetes) and B-cell malignancies. Further, the specification does not teach how to make *any* antibody as set forth in claim 1 having undisclosed amino acid residues in the framework of the heavy chain at the positions 49, 66, 76, 77 and 94 or the antibody as set forth in claim 1 having the undisclosed amino acid residues at position 64 of the framework of light chain because there is insufficient guidance as which undisclosed amino acid residues to be includes at those positions and whether the resulting antibody maintain the structure and binding specificity as the antibody set forth in claim 1.

11. Claims 1-10, 12 and 18-19are free of prior art.

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844 or (571) 272-0846 after January 20, 2004. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973 or (571) 272-0841 after January 7, 2003. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
December 29, 2003

Christina Chan

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